Art Unit: 1634

Attachment

1. The Reply Brief filed 11 December 2007 has been entered and considered but is not found persuasive for the reason(s) listed below.

A. In response to Appellant's arguments on pages 6-7 of the Reply Brief that "McGall, in full knowledge of nucleic acid hybridization, nevertheless explicitly teaches that the way to measure depurination is the direct chemical labeling of oligonucleotides and quantitation of how much label remains after exposure to a depurinating condition, while Weng teaches using two-channel measurement of hybridization signals on a good quality control array vs. a test array as a means to control the quality of microarray slide production. Neither reference teaches or suggests using hybridization as a means to test depurination.

However, as noted on pages 8-9 of the Examiner's Answer filed 11 October 2007, McGall teaches subjecting the arrays to one or more test conditions, wherein test conditions include operating conditions (column 11, lines 20-41), and wherein operating conditions of the array includes hybridization of nucleic acids to the array (column 13, lines 33-57). Thus, while McGall testing the array to detect depurination (i.e., as a test condition; column 9, lines 22-65), that more than one test condition is applied (column 11, lines 20-41), that test conditions include operating conditions (column 11, lines 20-41), and wherein operating conditions of the array includes hybridization of nucleic acids to the array (column 13, lines 33-57), McGall does not explicitly show hybridization as a test condition for determining depurination.

However, Weng et al teach a method of detecting the presence of nucleic acids; namely, measuring expression levels of nucleic acids using microarrays (column 8, lines 60-67). Weng et al also teach hybridization is used as a test condition (column 4, lines 58-67), and that hybridization as a test condition has the added benefit of providing a method of controlling the quality of the microarray production process (column 5, lines 29-32).

Use of the hybridization test condition of Weng et al in the method of McGall is thus interpreted as outlined in the single exemplary embodiment: two ensembles of oligonucleotides in two areas of an

array of McGall are both subjected to the same hybridization test condition of Weng et al. The ensemble in the first area is subjected to cleavage of depurination products. The amount of label at each site is detected and compared to determine the presence of depurination reaction products on the surface of the array. Thus, the resultant binding complexes of the uncleaved depurination probes with the target nucleic acid are compared to the cleaved binding complexes of the depurination probes with the target nucleic acid to determine the presence of depurination reaction products on the surface of the array.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the depurination detection test conditions as taught by McGall using hybridization as a test condition as taught by Weng et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in providing a method of controlling the quality of the microarray production process as explicitly taught by Weng et al (column 5, lines 29-32).

B. Appellant asserts on page 7 of the Reply Brief that the citation from McGall (column 10, lines 20-35) regarding "Rates of Depurination" has no relation to hybridization of probes or nucleotides.

However, it is noted that the citation describes "[v]arious conditions used in the synthesis of a chip can be tested for the extend to which they cause depurination. For example…." The phrase "for example" clearly indicated that the list of depurination conditions is not limiting and describes only several possible non-limiting embodiments that do not exclude hybridization as a test condition.

C. Appellant also argues on pages 7-8 of the Reply Brief that column 4, lines 58-67 of Weng et al teaches correction of hybridization patterns.

However, column 4, lines 58-67 of Weng et al is merely relied upon for use of the array in a hybridization assay, which is an example of operating conditions. Appellant is reminded that the operating conditions are test conditions according to McGall (column 11, lines 20-41). Thus, the operating conditions described by Weng et al in column 4, lines 58-67 are the operating conditions as test conditions of McGall et al.

D. Appellant further asserts on page 8 of the Reply Brief that the examiner has changed the operating principle of the primary reference and rendered McGall inoperable.

However, the arrays of McGall are clearly used for hybridization (column 13, line 34-60). Thus, the operating conditions of the array include hybridization conditions, and the operating principle has not been changed by the examiner. McGall is still operable because the array is used in the manner for which it was designed; namely, hybridization.

E. Appellant argues on page 9 of the Reply Brief that a mere description of "quality control" of array manufacture using "test conditions" in not sufficient to teach or suggest the instant claims because McGall suggest other ways to address quality control without explicitly teaching the use of hybridization.

However, as noted on pages 8-9 of the Examiner's Answer, McGall teaches subjecting the arrays to one or more test conditions, wherein test conditions include operating conditions (column 11, lines 20-41), and wherein operating conditions of the array includes hybridization of nucleic acids to the array (column 13, lines 33-57). Thus, while McGall testing the array to detect depurination (i.e., as a test condition; column 9, lines 22-65), that more than one test condition is applied (column 11, lines 20-41), that test conditions include operating conditions (column 11, lines 20-41), and wherein operating conditions of the array includes hybridization of nucleic acids to the array (column 13, lines 33-57), McGall does not explicitly show hybridization as a test condition for determining depurination.

However, Weng et al teach a method of detecting the presence of nucleic acids; namely, measuring expression levels of nucleic acids using microarrays (column 8, lines 60-67). Weng et al also teach hybridization is used as a test condition (column 4, lines 58-67), and that hybridization as a test condition has the added benefit of providing a method of controlling the quality of the microarray production process (column 5, lines 29-32).

Use of the hybridization test condition of Weng et al in the method of McGall is thus interpreted as outlined in the single exemplary embodiment: two ensembles of oligonucleotides in two areas of an

array of McGall are both subjected to the same hybridization test condition of Weng et al. The ensemble in the first area is subjected to cleavage of depurination products. The amount of label at each site is detected and compared to determine the presence of depurination reaction products on the surface of the array. Thus, the resultant binding complexes of the uncleaved depurination probes with the target nucleic acid are compared to the cleaved binding complexes of the depurination probes with the target nucleic acid to determine the presence of depurination reaction products on the surface of the array.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was claimed to have modified the depurination detection test conditions as taught by McGall using hybridization as a test condition as taught by Weng et al with a reasonable expectation of success. The ordinary artisan would have been motivated to make such a modification because the modification would have resulted in providing a method of controlling the quality of the microarray production process as explicitly taught by Weng et al (column 5, lines 29-32).

F. Appellant argues on pages 10-11 of the Reply Brief that Appellant does not agree that page 9 of the Appeal Brief filed 15 June 2007 states that the removal of depurination oligonucleotides and determination of the amount of depurination are test conditions according to McGall.

However, page 9 of the Appeal Brief states that "to the extent that McGall discloses determining the amount of depurination, it is with respect to subjecting the substrate to a test condition, and then determining the extent of any resultant depurination by quantitating any oligonucleotides which remain attached to the substrate." Thus, Appellant is, in fact, stating that test conditions include subjecting the substrate to a test condition, and then determining the extent of any resultant depurination by quantitating any oligonucleotides which remain attached to the substrate.

G. Appellant further argues that the examiner has changed the principles of McGall and rendered McGall inoperative.

However, as noted above, the arrays of McGall are clearly used for hybridization (column 13, line 34-60). Thus, the operating conditions of the array include hybridization conditions, and the operating

principle has not been changed by the examiner. McGall is still operable because the array is used in the manner for which it was designed; namely, hybridization.

H. Appellant asserts on pages 11-12 of the Reply Brief that claim 21 recites "a nucleic acid a nucleic acid ligand that specifically binds to said nucleic acid analyte with a sample suspected of comprising said analyte under conditions sufficient for binding of said analyte to said nucleic acid ligand on said array to occur," and further, "detecting the presence of binding complexes of said nucleic acid ligand and said analyte on the surface of said array," and that the ordinarily skilled artisan is well aware that hybridization is how "binding complexes of said nucleic acid ligand and said [nucleic acid] analyte" form, and that the claimed "depurination features" and "depurination probe" function to detect depurination by hybridization, particularly in light of the specification.

However, as noted on page 13 of the Examiner's Answer, independent claim 21 merely requires "detecting the presence of binding complexes of the **nucleic acid ligand** and the **analyte** on the surface of the array to detect the presence of the nucleic acid analyte in the sample" (emphasis added by the examiner). While the array also has depurination probes, **claims 21 and 23-25 do not require anything to bind to the depurination probe, nor is the binding used to determine the presence of depurination reaction products**. Thus, the alleged deficiency of McGall with regard to independent claim 1 is moot with regard to independent claim 21 because the determination of depurination is not within the scope of claim 21.

Further, although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Thus, the claim has been given the broadest reasonable interpretation consistent with the teachings of the specification regarding "detecting the presence of binding complexes" (*In re Hyatt*, 211 F.3d1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000) (see MPEP 2111 [R-1]).

2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert T. Crow whose telephone number is (571)272-1113. The examiner can normally be reached on Monday through Friday from 8:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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